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Steven Susaña-Castillo, EMD 2020

Neighborhood and Environmental Factors and the Relationship to the Willingness to Use and Actual Uptake of Pre-exposure Prophylaxis (PrEP) Uptake, a Rapid Scoping Review

Title: Neighborhood and Environmental Factors and the Relationship to the Willingness to Use and Actual Uptake of Pre-exposure Prophylaxis (PrEP) Uptake, a Rapid Scoping Review

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Abstract

PrEP (Pre-Exposure Prophylaxis), which appeared on the market after FDA approval in 2012, is more than 90% effective against HIV transmission via sexual contact and more than 60% effective against HIV transmission via intravenous drug use. Current interventions focus on individual behavior or clinical guidelines, however, there has been little focus on the environmental factors affecting PrEP willingness and uptake. To investigate the relationship between neighborhood, environmental factors and PrEP willingness and uptake in the United States, a rapid scoping review was conducted with three electronic databases of articles (January 2012 – March 2020). Of the 2,016 citations screened, 11 articles were ultimately chosen for this review. Although PrEP willingness and uptake have been increasing overall, Black and Latinx people and those who live in rural areas, the Midwest, and the South significantly lag in this trend. Moreover, themes captured in the neighborhood and environmental variables were physician access, physician stigma, and resource access. Future policy recommendations will need to acknowledge the neighborhood and environmental factors that lead to disparities in HIV prevention.

Acknowledgements

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Introduction

With HIV prevention interventions like Pre-Exposure Prophylaxis (PrEP), the focus has been on clinical aspects, like physician guidelines, as the factors responsible for the observed differences in PrEP uptake. However, little attention has been given to understanding the effects of the neighborhood and environment characteristics on PrEP willingness and uptake. It is likely that PrEP willingness and uptake differences are influenced by upstream social determinants of health and would require policy implementation addressing the underlying them to mitigate their effects.

HIV in the United States continues to be a major public health problem. In 2018, there were 37,831 new HIV cases identified in the United States.¹ The highest rate of infection by race was Black/African American at 39.3 cases per 100,000 persons compared to non-Hispanic white people at 16.2 cases per 100,000 persons.¹ Of new cases identified, men who have sex with men (MSM) accounted for roughly 69%, heterosexuals accounted for 24% and people who inject drugs accounted for 7%.¹ PrEP has largely been advertised to MSM because they account for a large swatch of new infections. PrEP is a once daily antiretroviral pill that combines tenofovir and emtricitabine which prevents HIV from engaging in viral replication processes.

Over the past decade, there have been medical advances that have improved the prevention and management of HIV. PrEP, which appeared on the market after FDA approval in 2012, is more than 90% effective against HIV transmission via sexual contact and more than 60% effective against HIV transmission via intravenous drug use.^{2,3} From clinical studies like iPrEx, PrEP's efficacy was found to be 92% and from IPERGAY, a clinical study

regarding intermittent use of PrEP for MSM found 86% efficacy against HIV transmission.^{2,4}

Currently, those without HIV who are sexually active MSM, sexually active heterosexual men and women, sexually active transgender people, people who inject drugs, and have been prescribed post-exposure prophylaxis (PEP) and continue to be at risk are clinically eligible for PrEP.⁵

Despite these medical advancements, those who would benefit most from PrEP are not necessarily the ones initiating PrEP use. Some estimates of overall PrEP use in the United States is 26 PrEP users per 100,000 persons.⁶ Further, PrEP uptake amongst Black MSM ranged from 5% to 11% but were much less likely to be on PrEP in comparison to their white counterparts even after adjusting for having an HIV positive sex partner, recent group sex, peer network size, and city.^{7,8}

HIV prevention has largely focused on increasing access to PrEP and rolling out educational campaigns to address the observed differences of HIV infection. These interventions' efforts may be undermined by more systemic problems, like unstable housing, stigma, unaffordable medical care, homophobia and difficulties traveling to care, that affect not only the likelihood of seeking medical care but the likelihood of adhering to PrEP enough for it to be optimally effective.⁹⁻¹²

The socioecological mode is useful for understanding HIV prevention and care.¹³ The push to understand HIV prevention in this context is to acknowledge that individual behaviors are informed by their social and physical environment. One study showed why this model is useful for understanding HIV prevention by interview rural African Americans

from North Carolina about their perceptions of multi-level HIV risk factors, community needs, and assets in order to identify areas for improvement.¹⁴ Participants identified interpersonal processes, community structural environment, social disorder, and civic engagement as being mediators to HIV risk. Further, they identified neighborhood poverty, lack of skilled jobs, segregation, political disenfranchisement, and institutional racism as barriers to combatting HIV in their neighborhoods. These types of studies could catalyze broader policy recommendations by identifying structural or environmental factors that indirectly impact an individual's access to HIV care.

Methods

Search Strategy

We searched PubMed, CINAHL, and EMBASE for articles published on or before April 3, 2020. We use broad search terms to encapsulate the concepts of pre-exposure prophylaxis (PrEP), uptake or willingness, and geography-related terms. [Appendix Figure 1](#) provides a more detailed search query guided by PRISMA guidelines. Additional studies were found by retrieving cited works in the selected articles.

Inclusion Criteria

Studies in the review were included if they met the following criteria: were focused on PrEP willingness and/or uptake and included analysis connecting geographic variables that may provide insight into neighborhood or community characteristics as predictors of willingness and/or uptake. Geographic variables in this review include variables that capture region, state, ZIP code, Census-level, city, urban, rural, suburban, and neighborhood factors. The population of focus for this review is in the United States. Studies were excluded if they were published before January 1, 2012 since PrEP became available in July 2012. Studies were additionally excluded if they were not written in English, focused on medical or biological aspects, focused on PEP or ART, or were editorials and comment letters.

Data Extraction and Management

Articles identified in the search were screened in several rounds by one person. First, duplicates in the final search pool were removed. Given that PrEP did not hit the market until July 2012, articles older than January 1, 2012 were removed. Articles that were not focused in the United States and/or not in English were removed. After that articles that were not

deemed relevant because they were clinical trials, pharmacological in nature, an editorial or comment letter, or were not focused on PrEP uptake or willingness. Full-text articles were extracted for the remaining studies. Data included in the studies: citation, study design/method, sample/population size, the population of focus, exposure, outcome(s), covariates, geographic variables, and findings related to the geographic variables.

Findings were separated by the outcome of interest, either PrEP willingness or PrEP uptake. Findings were then grouped by their type of geographic variable: region, rural/urban construct, city- or borough-level, county-level, and zip code-level.

Results

Description of Included Studies

[Appendix Table 1](#) presents details on the search and screening process. A total of 2,010 studies were identified through database searches. 586 studies were identified in PubMed, 104 studies were identified in EMBASE, and 1,320 studies were identified in CINAHL. Through citation searches in the identified articles, six articles were identified. Of the 2,016 studies, 1,888 studies were screened by title, abstract, and year. Full-text reviews were performed on 159 articles. Of those, 11 articles were deemed relevant for the review.

[Appendix Table 2](#) presents the characteristics of the studies included in the review. Of the 11 included studies, one was a qualitative study and 10 were quantitative studies. Eight studies focused on men who have sex with men (MSM) or gay and bisexual men (GBM), two studies focused on Black/African American individuals, two studies focused on the general population, one study focused on veterans, one study focused on MSM couples, and one study focused on recently HIV diagnosed. Four studies included PrEP willingness as an outcome, 10 studies included PrEP uptake as an outcome, and five studies included both as an outcome. Regarding geographic variables, seven studies included region variables, three studies included rural/urban constructs, two studies included city- or borough-level variables, one study included county-level variables, and one study included ZIP code-level variables. Only significant results are highlighted in the following section. Themes identified in the studies include healthcare access, physician stigma, and resource access.

PrEP Willingness and Uptake

MSM in the rural Midwest through semi-structured interviews identified PrEP being unavailable in rural areas, primary care physicians (PCPs) were unwilling to prescribe PrEP and held stigma against those who were seeking PrEP services as reasons for lack of PrEP willingness and use.¹⁵ The theme of the variable captured is related to physician stigma and healthcare access. Another study found that MSM who live in small/medium metropolitan areas compared to urban areas were 8% more likely to express PrEP willingness even though all regions saw increases to PrEP willingness.¹⁶ The variable captures information regarding the structures of large urban areas versus smaller and medium metropolitan areas that may present as barriers to PrEP willingness.

Black individuals who lived in the West were almost twice as likely to express PrEP willingness compared to those who lived in the Northeast.¹² The variables in this study capture healthcare access at the ZIP code level. This study took a creative approach when constructing ZIP code-level variables that include PrEP clinic density per 10,000 people, driving distance to PrEP clinic from population centroids, the density of doctors and outpatient clinics, density of community health centers (CHC), density of hospitals, density of clinics/CHCs/hospital composites, and proportion of Black/African American, unemployed, living in poverty and uninsured. For Black individuals, higher PrEP clinic density was associated with a 16% increased PrEP willingness.

MSM, in one study, who live in suburban, small/medium metropolitan and rural areas were 38%, 42%, and 55% less likely to report PrEP use compared to those who lived in urban areas, respectively.¹⁶ Another study focused on MSM reported that higher county-level median household income was associated with a 33% increase in PrEP use.¹⁷ When stratified

by race/ethnicity, white MSM were 23% and 21% more likely to use PrEP compared to Black and Latinx MSM in the South, and white MSM were 28% more likely to use PrEP compared to Black MSM in the West.¹⁸ Further, a study on MSM couples reported that those from the Northeast and West were 99% and 121% more likely to be a survey participant being the only partner on PrEP compared to those living in the South and that those from the Northeast and Other (e.g., United States possession or military overseas) were 70% and 492% more likely to have both partners being on PrEP compared to the South.¹⁹

The remaining study focused on veterans who use those newly diagnosed HIV positive in New York City. Amongst those newly diagnosed as HIV positive in New York City, those living in Queens were 88% less likely to report previous PrEP use than those who came from Manhattan.²⁰

Discussion

This review describes the limited studies conducted so far assessing the relationship between PrEP willingness and uptake with geographic variables that may elucidate neighborhood and environment characteristics important to closing gaps in the PrEP care continuum for all populations. Addressing the broader contexts that people live in can provide sustainable interventions by mitigating the structural factors associated with HIV. Also, given the disparities in HIV incidence among people who inject drugs and Black individuals in the United States, more studies are needed to understand the environments that lead to those disparities.²¹

Since the availability of PrEP in 2012, PrEP willingness and uptake have increased across the United States.^{16,22} This trend can be partially attributed to the various outreach and education activities to raise awareness of PrEP. Generally, studies reported higher PrEP uptake among West and Northeast regions compared to the Midwest and South.^{18,19,23} Future HIV prevention resources may need to be especially funneled into the Midwest and South given the differences in access to HIV prevention services.

Many studies that included PrEP willingness or uptake as an outcome of interest reported gaps for those who live in rural areas.^{12,15,16,23} The gap between PrEP willingness to PrEP uptake opens an opportunity for intervention. The themes identified by MSM in the rural Midwest in regards to lower initiation rates of PrEP regardless of PrEP willingness provide insight into the bottlenecks in HIV prevention services for those who live in rural areas.¹⁵

Only one of the studies incorporated neighborhood and ZIP code-level variables related to resources and access.¹² HIV interventions cannot solely rely on individual behavioral interventions and must be coupled with examinations of the resources available to communities for promoting health. This study produced innovative ways of thinking about area-level variables that could be assessed on other related HIV outcomes.

Limitations

This review highlights the scarcity of studies connecting geographic variables to PrEP uptake and willingness even when using broad search terms. Even among relevant articles, several studies either did not report the significance of findings or did not find many significant relationships related to geographic variables, which limits the number of items that were highlighted.^{16,17,19,22-25} The studies largely focused on MSM which leaves a gap of knowledge for other important populations like Black women or people who inject drugs. Moreover, limiting studies to the United States may miss opportunities to learn about geographic relationships from other countries that could be translated to the United States context.

Conclusion

PrEP has proven to be a powerful pharmaceutical intervention for preventing HIV. It is just one of many interventions currently being employed to tackle the HIV epidemic. The disparities in HIV incidence extend into PrEP willingness and uptake for those in rural areas and/or those who are Black/African American. Identifying the neighborhood and environment characteristics that facilitate these disparities will further increase HIV prevention and provide policy approaches that address the broader needs of those most at risk for HIV.

Appendix

Table 1. PubMed Search Terms

PrEP	Uptake	Willingness	Area-level
"PrEP"[tw]	"Uptake"	"willingness"	"location*"
OR	OR	OR	OR
"pre-exposure prophylaxis"	"Initiation"	"values"	"city"
OR	OR	OR	OR
"pre exposure prophylaxis"	"Initiat*"	"preference*"	"cities"
OR	OR		OR
"preexposure prophylaxis"	"Start*"		"state*"
OR	OR		OR
"Truvada"	"Begin*"		"count*"
OR	OR		OR
"tenofovir disoproxil fumarate-emtricitabine"	"Use"		"county-level"
OR	OR		OR
"TDF-FTC"	"Using"		"rural"
	OR		OR
	"Intake"		"metropolitan"
	OR		OR
	"Adopt*"		"MSA"
	OR		OR
	"Utiliz*"		"MSAs"
	OR		OR
	"Utilis*"		"urban"
	OR		OR
	"Commence"		"suburb*"
	OR		OR
	"access*"		"neighborhood*"
	OR		OR
	"prescription*"		"ZIP code*"
	OR		OR

	"Prescrib*"		"census tract*" OR "area-level" OR "region" OR "census block"
Pre-Exposure Prophylaxis [MeSH] Emtricitabine [MeSH] Tenofovir [MeSH] Emtricitabine, Tenofovir Disoproxil Fumarate Drug Combination [MeSH]		Attitude to Health [MeSH] Health Knowledge, Attitudes, Practice [MeSH] Patient Acceptance of Health Care [MeSH]	

Figure 1. Inclusion Criteria Flowchart

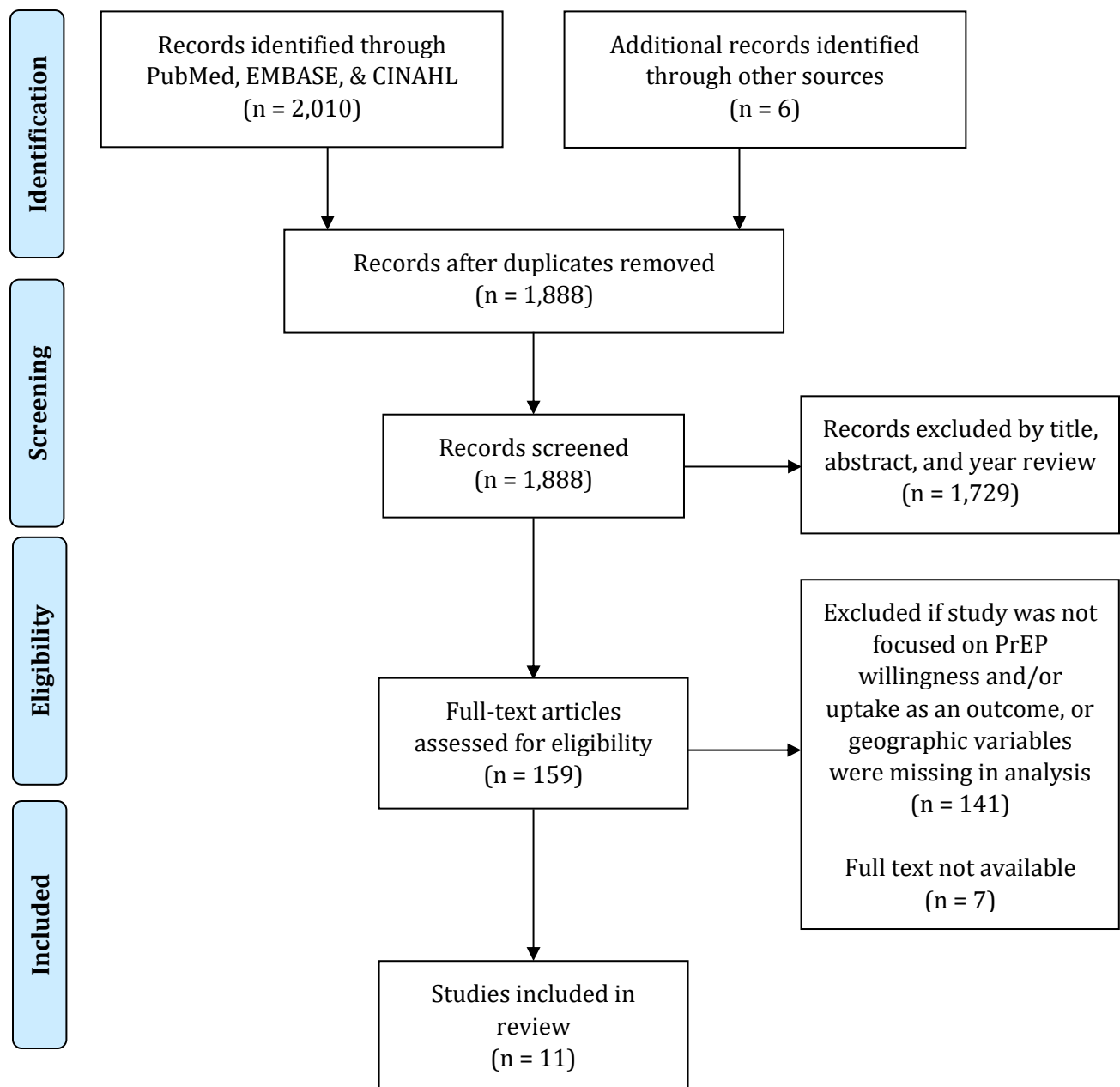


Table 2. Studies Included in Review

Reference	Study Design/Methods	Sample Size	Populations of Focus	Exposure	Outcome(s)	Covariates	Geographic Variable(s)	Findings
Duncan et al., 2019²⁴	Prospective longitudinal study	361	Black men who have sex with men (MSM)	Living in Chicago or "Deep South" (New Orleans, LA and Jackson, MS)	HIV status, HIV testing, HIV pre-exposure prophylaxis (Never taken, previously taken, currently taking), HIV treatment, HIV treatment adherence, recent condom use, sex work or transactional sex, group sex participation.	Age, ethnicity, sexual orientation, education, income, occupation, current living situation, nativity, relationship status, drug use, depression, past incarceration status, health insurance status, disclosure of same-sex behavior to primary care physician, residential self-selection, and residential history.	Chicago and "Deep South" (New Orleans, LA and Jackson, MS)	22.5% of those from Chicago and 26.1% of those from the "Deep South" were currently taking PrEP. No significant difference between the two locations.
Finlayson et al., 2019²²	Retrospective survey study	7,873	MSM	Cohort year	PrEP awareness and PrEP uptake.	Income, health insurance and region	Region (Midwest, Northeast, South, US territories, and West) and Urban area (Atlanta, GA; Baltimore, MD; Boston, MA; Chicago, IL; Dallas, TX; Denver, CO; Detroit, MI; Houston, TX; Los Angeles, CA; Miami, FL; Nassau and Suffolk counties, NY; New Orleans, LA; New York City, NY; Newark, NJ; Philadelphia, PA; San Diego, CA; San Francisco, CA; San Juan, PR; Seattle, WA; and Washington, DC).	All urban areas saw an increase of PrEP use. From 2014 to 2017, regions saw an adjusted prevalence ratio (aPR) from 3.91 to 6.26 and urban areas saw an aPR from 3.20 to 21.15. Significance was not assessed.

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Garner et al., 2018²³	Retrospective study; exploratory	825	Veterans who use the VA and are on PrEP	N/A	N/A	N/A	Region 1-5 (1: Connecticut, Delaware, Washington DC, Maine, Maryland, Massachusetts, New Hampshire, New Jersey, New York, North Carolina, Pennsylvania, Rhode Island, Vermont, Virginia, West Virginia. 2: Alabama, Florida, Georgia, Kentucky, South Carolina, Tennessee. 3: Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, Wisconsin. 4: Arkansas, Colorado, Louisiana, Mississippi, Montana, Oklahoma, Texas, Utah, Wyoming. 5: Alaska, Arizona, California, Hawai'i, Idaho, Nevada, New Mexico, Oregon, Washington).	Region 5 had the highest PrEP per capita initiation rate. Region 3 had the lowest PrEP per capita initiation rate. Outside of California, most PrEP initiations occurred close to or within larger cities. Significance was not assessed.
John et al., 2019¹⁹	Retrospective survey study; exploratory	3,140	HIV-negative or unknown HIV status MSM couples	N/A	Neither participant nor partner on PrEP, partner on PrEP only, participant on PrEP only, both participant and partner on PrEP, unknown partner PrEP use.	Age, sexual orientation identity, gender, race/ethnicity, education, region (South, Northeast, Midwest, West, Other), relationship arrangement with main partner, relationship duration with main partner, any condomless anal sex (CAS) with main partner in past 6 months, any CAS with male casual sex partners in past 6 months, sexual position identity,	Region (South as reference, Northeast, Midwest, West, Other like US possession and military overseas).	Compared to the South, those whose partners were on PrEP only were less likely to be from the Northeast and more likely from the Midwest and West. No significance was found. Compared to the South, those who were the only partner on PrEP were more likely to be from the Northeast, Midwest, West, and Other. Significance was found for the Northeast and West. Compared to the South, those with both partners on PrEP were more likely to be from the Northeast, Midwest, West, and Other. Significance was found for the Northeast and Other. Compared to the South, unknown HIV status PrEP use was more likely to occur in the Northeast,

						any bacterial STI diagnosis in the past 6 months, HIV status, main partner HIV status.		Midwest, West, and Other. No significance was found.
Kanny et al., 2019¹⁸	Retrospective survey study	4,056	MSM from urban areas	Race/ethnicity	PrEP awareness and use, discussion with a health care provider.	Age group, education, household income, currently have health insurance, usual source of health care when sick or need advice, bacterial STI within the past 12 months, anal sex without a condom within the past 12 months, HIV status of last sex partner, region (Midwest, Northeast, South, US territories, West).	Region (Midwest, Northeast, South, US territories, and West).	Compared to Black MSM, white MSM were more likely to be on PrEP regardless of region. Compared to Latinx MSM, white MSM were more likely to be on PrEP in the Midwest and South and were as likely or less likely to be on PrEP in the Northeast and West. Significance was found for the South and white MSM compared to Black MSM in the West.
Li et al., 2019¹⁷	Retrospective survey study; exploratory	8,338	MSM	N/A	PrEP awareness, willingness, and uptake.	Individual-level variables (age group, race/ethnicity, education, residence type, income, health insurance status, use of HIV behavioral interventions in the past 12 months, bacterial STI in the past 12 months, number of male partners in the past 12 months, male partner type in the past 12 months, condomless anal sex (CAS) in the past 12 months, CAS with HIV positive or unknown partner in the past 12 months)	County-level variables (proportion Black male, median household income, proportion of people uninsured, rescaled GINI coefficient, male HIV prevalence).	No evidence of geographic variation and PrEP willingness was found. The county-level proportion of Black male, proportion uninsured, and rescaled GINI coefficient were associated with higher levels of PrEP willingness, and county-level median household income and male HIV prevalence were associated with lower levels of PrEP willingness. Significance was not found. The county-level proportion of Black male, median household income, rescaled GINI coefficient were associated with higher levels of PrEP use, and county-level proportion uninsured and male HIV prevalence was associated with lower levels of PrEP use. Significance was found between county-level median household income and PrEP use.

						and county-level variables (proportion Black male, median household income, proportion of people uninsured, rescaled GINI coefficient, male HIV prevalence).		
Misra et al., 2019²⁰	Retrospective survey study; exploratory	3,718	Recently HIV diagnosed	N/A	Pre HIV diagnosis PrEP use.	Race/ethnicity, current gender, age group, New York City borough (Bronx, Brooklyn, Queens, Staten Island or outside New York City, Manhattan).	New York City borough (Bronx, Brooklyn, Queens, Staten Island or outside New York City, Manhattan).	Compared to Manhattan, individuals living in the Bronx, Brooklyn, Queens, and Staten Island or outside New York City were less likely to be on PrEP when diagnosed with HIV. Significance was found for those living in Queens.
Ojikutu et al., 2019¹²	Retrospective survey study	787	Black/African American individuals	PrEP density (PrEP clinics per 10,000 residents within a ZIP code)	PrEP willingness.	Individual-level variables (age, gender, education, income, insurance status, doctor visit, census region, metropolitan statistical area (MSA)) and ZIP code-level variables (proportion living in poverty, unemployed, and Black).	Individual-level variables (census region and MSA) and ZIP code-level variables (density of PrEP clinics per 10,000 people, driving distance to PrEP clinic from population centroid, the density of doctors and outpatient clinics, density of community health centers (CHC), density of hospitals, density of clinics/CHCs/hospital composites, proportion Black/African American, proportion unemployed, proportion living in poverty, proportion uninsured).	Compared to those who live in the Northeast, Black individuals from the Midwest, South, and West were more likely to express PrEP willingness. Compared to those who live in urban MSAs, those who live in rural MSAs are less likely to express PrEP willingness. Significance was only found for those who live in the West compared to the Northeast. Increased PrEP willingness was associated with ZIP codes that had higher PrEP clinic density, a higher density of clinics/CHCs/hospital composites, a higher proportion of Black/African American, unemployed, and uninsured. Decreased PrEP willingness was associated with ZIP codes where the driving distance to PrEP clinic was shorter than one hour compared to those who had at least 1-hour drive and where the proportion of living in poverty was higher. Significance was only found between PrEP clinic density and PrEP willingness.

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Owens et al., 2020¹⁵	Qualitative interview study; exploratory	34	MSM in rural Midwest	N/A	Experience with PrEP health care (22 semi-structured interview items).	N/A	Index of Relative Rurality.	Major themes identified from the interviews about the PrEP care continuum, which includes PrEP willingness and use, were that PrEP is unavailable in rural areas, PCPs unwilling to prescribe is a barrier, and that PCPs in rural areas hold a stigma against those seeking PrEP services which creates a barrier to PrEP uptake.
Parsons et al., 2017²⁵	Prospective longitudinal study; exploratory	995	HIV-negative gay and bisexual men	N/A	Motivational PrEP Cascade which includes PrEP willingness and use (10 items).	N/A	Region identified by reported ZIP code (Northeast, Midwest, South, West).	No significant geographic associations were found with the Motivational PrEP cascade milestones which include PrEP willingness and use.
Sullivan et al., 2020¹⁶	Retrospective survey study; exploratory	37,476	HIV negative or unknown status MSM	N/A	PrEP awareness, willingness, and uptake.	Age group, race/ethnicity, recruitment type, population density (urban, suburban, small/medium metropolitan, rural), health insurance, region (Northeast, Midwest, South, West, US-dependent areas), NHBS city resident (yes, no).	Population density (urban, suburban, small/medium metropolitan, rural), region (Northeast, Midwest, South, West, US-dependent areas), NHBS city resident (yes, no).	Compared to those who live in urban areas, those who live in suburban, small/medium metropolitan, and rural areas are more likely to express PrEP willingness. Significance was only found for those who live in small/medium metropolitan areas compared to urban areas. Compared to those who live in urban areas, those who live in suburban, small/medium metropolitan, and rural areas were less likely to report PrEP use. Significance was found for all the population density variables. Overall, PrEP willingness and use increased over time regardless of region or NHBS city residence, however, significance was not assessed.

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